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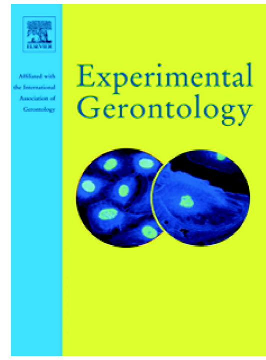

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Higher levels of objectively measured sedentary behaviour is associated with worse cognitive ability: Two-year follow-up study in community-dwelling older adults

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Running title: Objectively-assessed sedentary behaviour and cognitive ability

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Abstract (249/250)

Background

A number of cross-sectional studies have suggested that higher levels of sedentary (SB) are associated with worse cognitive abilities in older age. There is a paucity of longitudinal studies investigating this relationship utilizing objective SB. This study investigates the relationship between objective SB and future cognitive abilities in a cohort of older adults.

Methods

A longitudinal study over 22.12 ± 1.46 months including 285 community-dwelling older adults across 14 regions in Taiwan was undertaken. Cognitive ability was ascertained using a Chinese version of the Ascertain Dementia 8-item Questionnaire (AD8) and SB captured by 7 days accelerometer data. Multivariable negative binomial regression models adjusted for confounders were undertaken.

Results

274 community-dwelling older adults finished the study (age = 74.6 ± 6.2, % female = 54.4%). At baseline, 20.1% (n= 55), 48.5% (n= 133) and 31.4% (n= 86) of the sample engaged in high (>11 hours), medium (8-10.99) and low (<8 hours) of SB respectively. In the fully adjusted model, higher levels of SB were associated with an increased risk of worse cognitive ability at follow up (adjusted rate ratio (ARR)1.09 (95%CI:1.00-1.19), with the

strongest relationship evident in those engaging in over 11 hours of SB (ARR 2.27 (1.24-4.16). The relationship remained evident after adjusting for depressive symptoms and physical activity.

Conclusion

Our data suggests that objective SB, particularly when over 11 hours a day, is independently associated with worse cognitive ability over a two year period. Our data adds to the pressing reasons to reduced SB in older age.

Key words: Sedentary behavior, physical activity, cognition, cognitive ability, older age

Introduction

There is now robust evidence demonstrating that people are living longer, yet with more years with disability [1,2]. As the number of older people increases, the total number of people affected by reduced or impaired cognitive abilities such as subjective memory complaints [3], mild cognitive impairment and dementia is also anticipated to increase [4,5]. Given the deleterious impact of such cognitive deteriorations, including reduced independence, decreased quality of life, premature mortality, high levels of healthcare utilization and cost [4,6], there is a need to identify potentially modifiable risk factors.

There is widespread acceptance that physical activity is a modifiable risk factor for future cognitive decline [7,8]. In the medical literature, there is increasing recognition that high levels of sedentary behavior (SB) are independent from physical activity, associated with a range of deleterious outcomes such as cardiovascular disease, cancer and mortality [9,10]. There is however, a paucity of studies investigating SB and cognition in older adults[11]. Nonetheless, a recent systematic review found that SBmay be associated with reduced cognition in older age in cross sectional studies [12]. However, the authors [12] were unable to identify any published longitudinal study investigating the relationship between SBand cognitive impairment in older age. Since the publication of that systematic review, two recent prospective studies [13,14] have suggested that self-report SBis associated with worse cognition in older adults. Whilst helpful, both studies reliance on the use of self-report measurement of SB is not validated and has unconfirmed accuracy, particularly in the context of older people with impaired cognition. Thus, there is a need for studies relying on the use of more accurate and reliable objective means to identify the relationship between SBand cognitive ability in older age.

Given the aforementioned, we set out to conduct a prospective study investigating the relationship between objectively measured SBand cognitive ability in a cohort of community dwelling older adults.

Methods

Study design and sample

The current study includes data from a two-year follow-up study of a community-based project, conducted in Hunei District, Kaohsiung, the second largest city in Taiwan. This project was designed to examine the associations between objectively assessed physical activity and mental health among community-dwelling older adults [15]. Between August and October 2012 (baseline), 285 community-dwelling older adults (aged 65 or older, mean ± SD = 74.5 ± 6.1 years) were invited to take part in the study and were subsequently assessed using standardized face-to-face household interviews and accelerometry (see details below). Across 14 villages of Hunei District, approximately 20 people were recruited from each community center using quota sampling. Individuals were drawn based on a national distribution according to sex and age in 2011 [16]. The second-wave interviews were performed between May to July 2014. Among the baseline sample, 274 participants (96.1%) participated in the follow-up after an average of 22.12 ± 1.46 months [15]. The research was approved by the National Taiwan University of Sport Institutional Review Board ethical committee (reference number: NTUPES-HSC-100-09). All participants provided written informed consent.

Measures

Cognitive ability

Cognitive ability was captured with the Chinese version of the Ascertain Dementia

8-item Questionnaire (AD8) [17,18]. Respondents were requested to rate changes in memory, orientation, problem-solving abilities, and daily activities (yes=1, no=0) with a potential range between 0 and 8. A higher score indicated a worse cognitive ability on the AD8 [17,19]. The AD8 has demonstrated adequate reliability and validity among community-dwelling Taiwanese older adults has been verified [20]. Within the current sample, the Cronbach's alpha for the AD8 ranged between 0.79 (first-wave) and 0.81 (second-wave).

Accelerometer-assessed sedentary time

The amount of time spent in SB was assessed using triaxial accelerometry (GT3X+, ActiGraph, Pensacola, FL, USA). Participants were instructed to wear the accelerometer on an elastic band on their waist at all times for 7 days, including 5 weekdays and 2 weekend days. In data analysis, a minimum of 10 hours of monitoring on a minimum of 5 days was required for data inclusion [21]. If the accelerometer had recorded data contained less than 5 valid days or had malfunctioned during wearing period, participants were requested to re-wear the accelerometer [22].

To get a better understanding on the relationships between SB and cognitive ability, the time spent in SB was then computed and converted into both continuous (hours/day) and categorical forms such as high (11+ hours/day), medium (7-10.99 hour/day), and low (< 7 hours/day). The cut-off-pints were based on previous research suggesting that the cut-off point for risk be as low as 7 or 8 hours a day and being sedentary for more than 11 hours a day may impair health [23]. Physical activity parameters such as time spent in moderate-to-vigorous physical activity was also estimated and recoded as a covariate (150+ min/week: no vs. yes) for multivariable adjustment [25,26].

Covariates

Underlying covariates were identified and assessed at baseline based on previous reviews [27-29]: comprising (1) socio-demographic variables: age, gender, years of formal education, marital status, and source of income (self [pension/savings)] vs. offspring), which may reflect adult children's social and financial support. Adult children provide remittances may increase older parents' financial stability and improve their mental well-being [30,31]; (2) lifestyle factors: time spent in moderate-to-vigorous physical activity, smoking, alcohol consumption, and; (3) health and chronic diseases: weight status category using body mass index (BMI) (<18.50, 18.50-23.99, 24-26.99, 27+),[32], number of comorbidities (0, 1, 2+) including hypertension, stroke, diabetes, heart disease, cancer, chronic obstructive pulmonary disease, liver disease, renal disease, and arthritis etc.; depressive symptoms assessed by the 15-item Geriatric Depression Scale (GDS) using cutoff of 5 (yes vs. no), [33,34]; and difficulties with activities of daily living (ADLs, no difficulties at all vs. some or great difficulties); (4) cognitive ability at baseline; (5) mean accelerometer wear time (hours/day) [35].

Data analysis

The sample size of the original study was determined for cross-sectional group comparisons. We therefore performed a post-hoc power analysis for negative binomial regression models using version 11.0 of Power Analysis and Sample Size Software (NCSS 2011, Kaysville, UT) for the longitudinal analysis. After adjusting for R-squared and over-dispersion parameter with the mean exposure time of 2 years, the total sample of 274 participants achieved 91.40% power at a 0.05 significance level to detect an incidence rate ratio of 1.53 (i.e. the average rate ratio based on our fully adjusted models).

The characteristics of the study sample were described using descriptive statistics. Mann Whitney U tests and Kruskal-Wallis tests were employed to examine the differences in cognitive ability in 2014 (follow-up) between categories of sedentary time and covariates in 2012 (baseline) due to the violation of normality. Variables with a p value (< 0.05) were then included in the subsequent multivariable regression models for adjustment.

To explore the simple correlations between objectively assessed SB (continuous and categorical) and cognitive ability in 2012 (baseline) and 2014 (follow-up) after adjusting for accelerometer wear time, partial correlation coefficients were calculated. Variables with a p value (< 0.05) were then included in the subsequent multivariable regression models for adjustment.

Given that the outcome variable was an over-dispersed count with a highly skewed distribution, multivariable negative binomial regression was conducted. To assess the potential confounding effect and reverse causality bias, four separate models were conducted to assess the prospective associations between SB (continuous and categorical form) and cognitive ability. The first model was adjusted for age, gender, and accelerometer wear time (Model 1). Then, years of education, marital status, income, number of comorbidities, and depressive symptoms were further included into the second model (Model 2). Because activities of daily living and moderate-to-vigorous physical activity were both related to physical function, which may influence SBat baseline and subsequent cognitive ability, the third model further included the two variables for test the confounding effect (Model 3). Finally, sensitivity analysis was carried out to test for the potential reverse causality bias of physical limitations on the associations of SBwith subsequent cognitive ability, the model 3 was conducted again after removing those with difficulty in activities of daily living at baseline (n= 13) (Model 4).

All analyses were conducted using IBM SPSS 20.0 software and a p value < 0.05 was considered statistically significant.

Results

From the 285 people at baseline (mean ± SD = 74.5 ± 6.1 years), 274 community-dwelling older adults completed the follow up assessment. Full details of the baseline information of the participants is illustrated in table 1. Regarding physical activity, most (86.9%) did not comply with the recommended 150 minutes of moderate to vigorous physical activity. One fifth (20.1%), almost half (48.5%) and 31.4% of the sample engaged in high (>11 hours), medium (8-10.99) and low (<8 hours) of SB respectively. Participants who were older, female, with a lower level of educational attainment, widowed/divorced, and whose income source were pension/savings, and had mild or severe comorbidities or depressive symptoms and experienced difficulty in activities at baseline were more likely to have lower levels of cognitive ability follow-up ($p < 0.05$). Individuals who spent more time in SB or did meet the recommended 150 minutes of moderate to vigorous physical activity in 2012 had poorer cognitive ability in 2014.

Table 1 here

Table 2 shows the partial correlations between time spent in SB coded as a continuous and categorical form and cognitive ability at baseline, and subsequent cognitive ability. After adjusting for accelerometer wear time, partial correlation coefficients demonstrated that higher levels of time spent in SB at baseline were cross-sectionally and longitudinally associated with worse cognitive ability regardless of SB coded as a continuous or categorical form ($p < 0.05$).

Table 2 here

The age-sex adjusted regression models demonstrated that SB as a continuous variable was significantly associated with worse future cognitive ability (model 1). The associations were slightly attenuated, but the pattern remained after further adjusting for other underlying covariates (model 2) and moderate-to-vigorous physical activity (model 3). The sensitivity analysis supported this association even after excluding participants with difficulty in activities of daily living. Notably, when SB was coded as a categorical variable, only those engaging in the highest amount of SB (> 11 hours/day) were significantly more likely to have worse cognitive ability compare to the least sedentary, which was consistent across the four models (see table 3).

Table 3 here

Discussion

To the best of our knowledge, the current study is the first to prospectively examine the association between objectively measured SB and cognitive ability in a cohort of community dwelling older adults. Our study found that higher levels of objective SB were independently associated with worse cognitive ability over the course of the study follow up. The relationship was independent of various potential confounding factors, including physical activity, depressive symptoms and difficulties with ADL. Moreover, our categorical analysis suggests that this effect is most pronounced in those engaging in over 11 hours of SB.

A recent systematic review [12] was unable to identify any longitudinal study capturing objective SB and cognitive impairment, however, it was noted from cross sectional and self-report data that SB may be related to worse cognition. The authors [12] made recommendations that future research is required to understand the potential long term influence of SB and cognitive status and in particular attempt to explore if any affect is evident after adjusting for physical activity. However, there is some recent evidence from two studies relying on self-report SB [13,14], which have suggested that engaging in higher levels of SB is associated with worse cognitive outcomes. Our data provide the first evidence that higher levels of objectively assessed SB are associated with worse cognitive abilities in a cohort of community older adults, helping to advance the literature from the recent cross sectional and self-report research in this area. The potential reasons why SB may negatively influence cognitive ability in older age are not clear at this early stage. There has been speculation that the established negative impact of SB on glucose metabolism, diabetes risk, obesity and cardiovascular disease [9,36,37] (all of which are also risk factors for cognitive impairment) could potentially act as mechanisms which subsequently increase the risk of cognitive abilities in older age. It may also be posited that the unfavorable inflammatory profile associated with SB reported in working age adults [38,39], including increased c-reactive protein (CRP) or interleukin -6 (IL6) [38,39] and confirmed in recent randomized controlled trials [40,41], could contribute to the potential cognitive deterioration we observed [42]. Despite this evidence of the deleterious outcomes of SB in working age adults, a recent systematic review found very few studies had investigated such underling biochemical or neurobiological markers specifically in older adults [43]. Thus, clearly future research is required to explore such hypothesis. There is a growing body of evidence to suggest that sedentary behavior is also associated with depression [44], which is another risk factor that has been associated with worse cognition in older age [45]. In the crude analyses at baseline, we found some evidence that SB was associated with depression but the relationship between SB and cognitive ability remains robust after adjusting for depression scores, thus indicating some potential independent relationship in our sample between SB and cognition.

Given the findings of our study and the wider literature considering the deleterious impact of SB on multiple health outcomes [9], it is essential that older adults seek to limit SB time and future studies should consider the cognitive impact of such interventions. This could include interrupting periods of prolonged SB and specifically increasing light physical activity which has favourable cognitive benefits [46]. A number of promising interventions are currently underway testing novel strategies to reduce SB in older adults including the use of behavior change techniques [47,48] and a large multi-country self-management and exercise referral scheme [49]. Such interventions will provide important evidence for the expanding elderly population to reduce SB.

Whilst our data are novel, and address an important gap within the literature it is important to note the observational nature of the data, precluding any indication of a causal link. Thus, clearly further longitudinal research is required to confirm/ refute our findings. Another important limitation is that we did not make the distinction between different types of SB, which may be associated with cognition to differing degrees. Thus, future longitudinal research should for instance attempt to explore the relationship between cognitively active SB (e.g. reading) and cognitively inactive SB (e.g. TV viewing) and overall cognitive abilities in older age. In addition, future interventional work should seek to investigate the impact of changing SB levels of cognition. Moreover, the number and length of breaks in total sedentary time should be considered in future studies given that prolonged unbroken bouts of sedentary behaviors are found to yield more detrimental health effects than those with short and interrupted break [50]. Whilst we recruited participants from 14 different sites, the data is only from one country. Nonetheless, strengths of our paper include the objective measurement of SB, the longitudinal design and the fact that we adjusted for multiple underlying confounders (e.g. baseline cognitive status, depressive symptoms, ADL difficulties and physical activity) all of which can influence both SB and cognitive abilities.

In conclusion, in the current study we observed that higher levels of SB were associated with a deterioration in cognitive abilities in a multi-site cohort of community dwelling older adults. The greatest deterioration in cognitive abilities was in those older people who were sedentary for over 11 hours per day. These relationships appear to be independent of confounders such as ADL difficulties, depressive symptoms and physical activity, among others.

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Conflict of interest statement

The authors confirm that there are no financial conflicts of interest associated with this paper.

Table 1 Characteristics of participants aged 65 or older in 2012 (baseline) with cognitive ability in 2014

Variables at baseline	n= 274 (%)	Cognitive ability (Mean ± SD)	*p*-value[a]
Demographic			
Age			0.001
75+	43.1	1.45 ± 1.74	
65-74	56.9	0.81 ± 1.22	
Gender			0.003
Female	54.4	1.29 ± 1.61	
Male	45.6	0.85 ± 1.31	
Years of formal education			0.002
No formal schooling	41.2	1.27 ± 1.66	
6 years	41.2	1.17 ± 1.49	
9 years or more	17.6	0.46 ± 0.82	
Marital status			0.002
Widowed/divorced/unmarried	29.9	1.48 ± 1.71	
Married	70.1	0.92 ± 1.37	
Source of income			0.001
Self (pension/savings)	49.3	1.35 ± 1.61	
Offspring	50.7	0.83 ± 1.37	
Lifestyle			
Sedentary time (hours/day)			0.001
High (11+)	20.1	1.95 ± 1.90	
Medium (7-10.99)	48.5	1.05 ± 1.45	
Low (< 7)	31.4	0.62 ± 1.66	
Moderate-to-vigorous PA (≥150 min/week)			0.006
No	86.9	1.18 ± 1.47	
Yes	13.1	0.45 ± 1.49	
Smoking			0.122
Former smoker	5.1	1.71 ± 1.77	
Current smoker	8.0	1.36 ± 1.65	
Never smoker	86.9	1.03 ± 1.46	
Alcohol consumption			0.696
Yes	4.7	1.31 ± 1.75	
No	95.3	1.08 ± 1.49	
Health and chronic disease			

Weight status (body mass index)			0.888
Underweight (<18.5)	4.0	1.18 (1.78)	
Normal (18.5-23.99)	36.9	1.06 (1.26)	
Overweight (24-26.99)	36.9	1.12 (1.70)	
Obese (27+)	22.2	1.07 (1.47)	
Number of comorbidities			0.041
2 or more	19.0	1.52 (2.00)	
1	38.0	1.13 (1.37)	
0	43.0	0.86 (1.30)	
Depressive symptoms			0.018
Yes	17.9	1.53 (1.78)	
No	82.1	0.99 (1.41)	
Activities of daily living			0.012
Some or great difficulties	95.3	2.23 (2.13)	
No difficulty at all	4.7	1.03 (1.44)	

PA: physical activity

a: Mann Whitney U test or Kruskal-Wallis test

Partial correlation analyses between sedentary time and subsequent cognitive ability

Table 2 Partial correlation coefficients between baseline sedentary time parameters and cognitive ability at follow-up adjusting for mean daily accelerometer wear time (n=274)

Variables	Baseline			Follow-up
	1	2	3	4
1. Sedentary time (categorical)[a]	1.00			
2. Sedentary time (continuous)[b]	0.74***	1.00		
3. Cognitive ability (baseline)	0.24***	0.15*	1.00	
4. Cognitive ability (follow-up)	0.24***	0.21***	0.45***	1.00

a: Low (< 7 hours)= 1, medium (7-10.99 hours)= 2, high (11+ hours)= 3

b: Hours per day

*p< 0.05, ** p< 0.01, *** p < 0.001

Multivariable associations between sedentary time and subsequent cognitive ability

Table 3 Negative binomial regression models examining the adjusted effects of time spent in sedentary behaviors at baseline on subsequent cognitive ability

Sedentary time (hour/day)	Model 1 (n=274)		Model 2 (n=274)		Model 3 (n=274)		Model 4(n=261)	
	ARR (95% CI)	*p*	ARR (95% CI)	*p*	ARR (95% CI)	*p*	ARR (95% CI)	*p*
1. Categorical		0.001		0.006		0.036		0.026
High (11+)	2.50 (1.50-4.17)	< 0.001	2.41 (1.40-4.17)	0.002	2.10 (1.19-3.72)	0.010	2.27 (1.24-4.16)	0.008
Medium (7-10.99)	1.24 (0.90-1.69)	0.189	1.29 (0.93-1.80)	0.134	1.27 (0.90-1.79)	0.169	1.26 (0.89-1.80)	0.197
Low (<7)	1.00		1.00		1.00		1.00	
2. Continuous	1.13 (1.04-1.22)	0.002	1.11 (1.02-1.20)	0.020	1.10 (1.01-1.20)	0.026	1.09 (1.00-1.19)	0.047

ARR= adjusted rate ratio

Covariates in model 1: baseline cognitive status, sex, age, and wear time of accelerometer

Covariates in model 2: Covariates in model 1 and years of formal education, marital status, income source, smoking, number of comorbidities, depressive symptoms, and wear time of accelerometer

Covariates in model 3 (fully adjusted model): Covariates in model 2 and moderate-to-vigorous physical activity, and activities of daily living

Model 4 (sensitivity analysis): Based on model 3, participants (n=13) who had difficulty in activities of daily living were further excluded.

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Highlights

- First prospective study to investigate objectively sedentary behaviour (SB) and cognition in older adults.
- Higher levels of objective SB independently associated with worse cognitive ability over two years.
- This relationship was most pronounced in older people spending over 11 hours a day being sedentary.